RWD39

Using Linked Databases to Explore Healthcare Resource Use and Real-World Outcomes in a Rare Disease: Fabry Disease in England

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BACKGROUND

- Fabry disease (FD) is an X-linked lysosomal storage disorder which leads to a deficiency in α-galactosidase A.
- FD is associated with severe multi-organ dysfunction (cardiovascular, renal, respiratory, gastrointestinal systems and skin) and premature death.[1]
- The prevalence of FD varies between 1/3,100 people and 1/117,000 people in Europe. Some of the variation in prevalence is likely due to its underestimation because of the broad spectrum of clinical phenotypes.[2]
- There is limited real-world evidence on the epidemiology of FD and associated burden on the National Healthcare System (NHS) in England.[3]

Objectives

- To estimate the incidence and prevalence of FD
- To describe demographic and clinical characteristics and healthcare resource utilisation (HCRU) and associated cost in patients diagnosed with FD
- To estimate the survival in patients diagnosed with FD

METHODS

- This non-interventional, retrospective cohort study used the Clinical Practice Research Datalink (CPRD)[4] linked at patient level to the Hospital Episode Statistics (HES).[5]

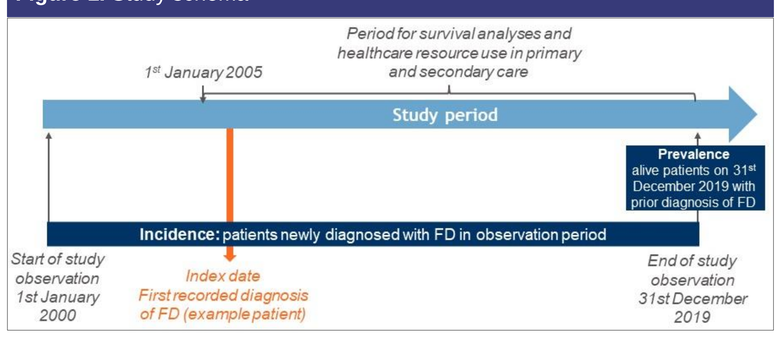
Data Source

- CPRD is a real-world research service that collects anonymised patient data from a network of general practitioner (GP) practices across the UK.
- HES is a secondary care data warehouse containing details of all admissions, outpatient appointments and accident and emergency attendances at hospitals in England.
- Mortality data was obtained through HES database linked to the Office for National Statistics database.[6]

Study Observation Period

- Starting on 1st January 2000 and ending on 31st December 2019
  - For analyses describing patients' symptoms, baseline observation period was defined starting at patient's registration into the database and ending on the date of first recorded diagnosis of FD (index date)

Figure 1. Study schema



Inclusion Criteria

- Permanently registered acceptable patient in CPRD (sufficient quality to be involved in research studies)
- FD diagnosis anytime prior or during the study observation period in CPRD
- Patient with ≥365 days follow-up at any point in time after the first recorded diagnosis and prior to 31st of December 2019
- For objective 1:
  - For incidence estimates, only patients with the first recorded FD during the study observation period
  - For prevalence estimates, only patients alive on the 31st December 2019

Exclusion Criteria

- Patient with a diagnosis of Pompe disease recorded in CPRD during or before the study observation period

Statistical Analyses

- Categorical variables were described with frequencies and percentages and quantitative variables with arithmetic means and standard deviation (SD).
- Healthcare resource use and cost-estimates were reported per patient-year. Costs were estimated using Personal Social Services Research Unit reference costs[7] for primary care and NHS tariffs[8] for secondary care.
- Incidence was estimated by dividing the number of newly recorded diagnoses of FD in a calendar year by the mid-year total study population.
- Prevalence was estimated on the 31st December 2019 as a point-prevalence counting all patients with FD diagnosis on or prior to 31st December 2019 and who were alive on that date; and dividing by the total study population on that date.
- Survival was summarised as 5-year and 10-year survival and 95% confidence intervals (CI) and represented using Kaplan-Meier survival plot.

RESULTS

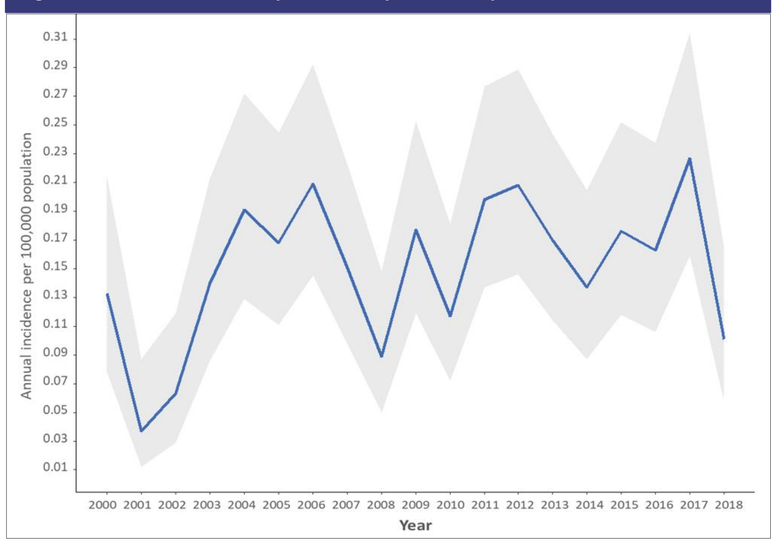
Study Population

- A total of 535 patients (mean age of 37 years) diagnosed with FD during the study period were identified in CPRD
- Linked primary and secondary data was available for 311 patients

Incidence and prevalence of FD

- Incidence of FD was 0.152 (0.139-0.167) per 100,000 persons (Figure 2)
- 492 patients were alive on 31st December 2019 providing a point prevalence of 3.69 (3.37-4.04) per 100,000 persons

Figure 2. Incidence of Fabry disease by calendar year



Grey area shows 95% confidence intervals (using the exact method)

Clinical Characteristics (Table 1)

- The majority of patients were first diagnosed in adulthood, at a mean age of 37 years.
- Pain, respiratory, and mental health symptoms were the most frequently reported symptoms.
- Mean most recently recorded weight was 72.2 kg (SD: 20.4).

Table 1. Baseline characteristics

Patients' characteristics	Total cohort (n=535)
Age at first diagnosis of FD, years, Mean (SD)	37 (20)
Weight, kg, Mean (SD)	72.2 (20.4)
Symptoms, n (%)	
Neurological	78 (14.6%)
Pain	262 (49%)
Respiratory	174 (32.5%)
Gastrointestinal	118 (22.1%)
Renal	49 (9.2%)
Cardiovascular	87 (16.3%)
Mental health	123 (23%)
Skeletal	18 (3.4%)
Dermatological	92 (17.2%)

FD, Fabry disease; SD, standard deviation; n, number of patients.

Primary HCRU (Tables 2-3)

- Patients had 5.6 (SD 7.1) GP appointments (associated cost of £185 [SD 234]) and 33.1 (SD 50.5) primary care prescriptions (associated cost of £296 [SD 772]) per patient-year.
- Cardiology was the most frequent referral department.
- Ten most frequent referral departments post diagnosis of FD were (in order): cardiology; ear, nose & throat; physiotherapy; orthopaedic; for further care; gastroenterology; ophthalmology; gynaecology; dermatology; musculoskeletal

Table 2. Primary HCRU and associated costs (in GBP) for all patients, per patient-year during follow-up

HCRU, Mean (SD)	Fabry disease (n= 535)
GP visits	5.6 (7.1)
Consultations*	9.4 (11.7)
GP referral to secondary care	0.5 (0.7)
Prescription†	33.1 (50.5)
Cost, £, Mean (SD)	
GP visits	185 (234)
Consultations	203 (251)
Prescription	296 (772)

* Consultations were defined as a recorded contact with a healthcare professional including general practitioners or other allied professionals (e.g.: nurse, physiotherapist); † Primary healthcare prescribing was summarised as total number of prescriptions per patient year and included any issued prescription, repeat or acute; GP, general practitioner; SD, standard deviation.

Table 3. Number of patients with a primary care prescription during follow-up, organised by BNF Chapter

Primary care prescription, n (%)	Patients with FD (n= 535)
Central nervous system	390 (72.9%)
Respiratory system	370 (69.2%)
Gastrointestinal system	295 (55.1%)
Stoma appliances	288 (53.8%)
Ear, nose & oropharynx	278 (52%)
Cardiovascular system	236 (44.1%)
Nutrition& blood	236 (44.1%)
Malignant disease & immunosuppression	234 (43.7%)
Infections	188 (35.1%)
Eye	175 (32.7%)

BNF, British National Formulary; BNF is organised into Chapters and all NHS prescribed primary care treatment are listed in the BNF.

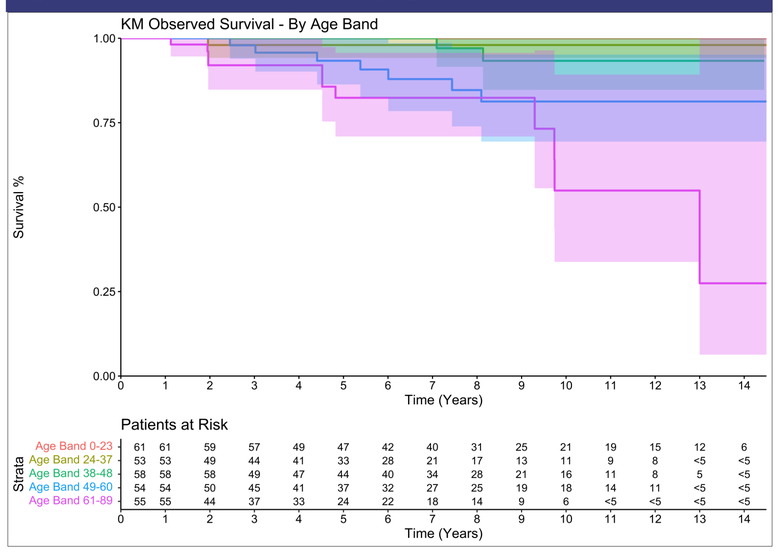
Table 4. Secondary HCRU and associated costs (in GBP) for all patients, per patient-year during follow-up

HCRU, Mean (SD)	Patients with FD (n= 535)
Outpatient visit	2.7 (4.2)
Inpatient admissions	0.9 (8.8)
Non-elective admissions	0.1 (0.5)
Elective/day case admissions	0.8 (8.7)
Critical care admissions	5 (0.9)
Accident and emergency attendances	0.2 (0.7)
Cost, £, Mean (SD)	
Outpatient visit	239 (367)
Inpatient admissions	
Non-elective admissions	187 (1,013)
Elective/day case admissions	246 (941)
Critical care admissions	2 (49)
Accident and emergency attendances	34 (106)

Secondary HCRU (Table 4)

- 55.3% of the patient had at least one outpatient visit (a mean of 2.7 [SD 4.2] visits per patient year) during follow-up
- 41.1% of the patients had at least one admission during follow-up (a mean of 0.9 admission [SD 8.8] per patient-year)
  - The majority of these admissions were day-cases or elective admissions
- Less than 1% of the patients had a critical care admission during the study period therefore the mean cost of these spells across the cohort was low.
- A third of the patients had accident and emergency attendance during observation with a mean number of 0.2 (SD 0.7) attendances per person year and £34 (SD 106) per patient year.
- The length of stay in hospital was highest in non-elective admissions (0.8 day in average, SD 4.4)

Figure 3. Kaplan-Meier survival plot by age bands (quintals)



- Overall survival was 95.3% (95% CI: 92.6-98.1) at 5 years and 87.8% (95% CI: 82.5-93.5) at 10 years from first recorded diagnosis.
- An exploratory analysis showed that 10 years survival decreased with the increase in age band indicating age at diagnosis is likely a predictor of OS (Figure 3).

LIMITATIONS

- Due to rarity of the diseases, low numbers of patients are available for research even from large datasets; small numbers raise the likelihood of biased estimates driven by outliers.
- Validity and completeness of individual patient records cannot be assessed due to the nature of electronic health records data. Therefore, there is some uncertainty in these results. Moreover, the study did not consider the impact of phenotype or earlier symptom onset on FD prognosis.
- Only patients with ≥365 days of follow-up post-index date during the study observation period were included in the analyses, therefore estimates of incidence and prevalence may have been underestimated.
- Linkage between the two databases resulted in a loss of data. However, in our study, all patients included were registered with an English postcode, therefore secondary healthcare resource use could be evaluated assuming that patients not linkable to HES did not have any secondary care use during the observation period.

CONCLUSIONS

- **The incidence and prevalence of FD as recorded in primary care electronic healthcare records were low and most patients were diagnosed in adulthood.**
- **10-year survival was 87.8% for the entire cohort, however there was large variation depending on age of FD diagnosis with patients diagnosed at an earlier age having poorer prognosis.**
- **FD is a rare condition; however, combined primary and secondary datasets highlight the substantial burden of Fabry disease and its impact on patients' quality of life, in particular regarding pain and mental health.**

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DISCLOSURES

- SB and DH: Employees of OPEN Health, which has received consulting fees from Sanofi
- MK, PD, SC, and PS: Employees of Sanofi
- Fatemeh Saberi Hosnijeh and Myriam Alexander, of OPEN Health company, provided medical writing support.

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